ORIGINAL ARTICLE

Plasma PCSK9 level is unrelated to blood pressure and not associated independently with carotid intima–media thickness in hypertensives

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Proprotein convertase subtilisin/kexin type 9 (PCSK9), a novel target for low-density lipoprotein cholesterol (LDL-C)-lowering therapy, has been found to possess multiple off-target effects in humans. The aim of the present study was to investigate the association of blood pressure (BP) with plasma PCSK9 levels in a large Chinese cohort and the relation of PCSK9 level to carotid intima–media thickness (cIMT) in hypertensive patients. A total of 805 patients without lipid-lowering drug therapy were consecutively enrolled. First, the relationship between BP and PCSK9 was evaluated in hypertensives and normotensives. Furthermore, we examined the relation of PCSK9 to cIMT in 256 enrolled patients who had received a carotid ultrasound test. Plasma PCSK9 levels were measured by enzyme-linked immunosorbent assay, and cITM of left and right carotid arteries was assessed by B-mode ultrasound. There was no significant difference in PCSK9 levels between hypertensives and normotensives. PCSK9 level was not associated with systolic and diastolic BP and pulse pressure in hypertensives and normotensives regardless of sex. A positive correlation between PCSK9 and maximum-IMT and mean-MIT in hypertensives was found in univariate analyses, whereas such an association was absent in normotensives. In addition, the positive association of PCSK9 with cIMT disappeared in hypertensives in multivariate analyses. PCSK9 level is not associated with systolic or diastolic BP in hypertensives or normotensives, but it positively correlates with cIMT in hypertensives in univariate but not multivariate analyses, and further researches are needed.

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INTRODUCTION

Dyslipidemia and hypertension are not only the manifestations of metabolic syndrome,[1] but also the well-established risk factors for coronary artery disease.[2–4] During the past decade, increasing evidence from epidemiological observations and prospective clinical studies has indicated that elevated serum total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels are associated with an increased risk of new onset of arterial hypertension.[5–10] On the other hand, it has been demonstrated that the reduction of serum cholesterol levels decreases blood pressure (BP).[11]

Proprotein convertase subtilisin/kexin type 9 (PCSK9), a secretory protease produced by the liver, is a major regulator of LDL-C by binding to hepatic LDL receptor and promoting their degradation, thereby leading to increased LDL-C concentrations.[12–14] Recently, several large clinical trials have demonstrated that PCSK9 monoclonal antibody can significantly reduce LDL-C levels.[15–17] In view of the

association between LDL-C and the risk of new onset of hypertension or BP values, it seems reasonable to speculate that PCSK9 may affect the development of hypertension or BP control. Furthermore, it is important to address the issue because it may predict whether the promising PCSK9 inhibitors bring a potential effect on hypertension or BP control.

Actually, the association between PCSK9 and hypertension or BP remains controversial. In the Dallas Heart Study, a positive correlation was found between PCSK9 level and both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in women but not in men.[18] Cui et al.[19] reported that PCSK9 was positively associated with SBP and DBP in both men and women. On the contrary, Berger et al.[20] found that PCSK9 deficiency did not alter BP in mouse models of hypertension. Similarly, in a recent nested case–control study with healthy American women, Ridker et al.[21] showed no association between PCSK9 and SBP and DBP. However, in most of previous

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studies, the enrolled participants were under lipid-lowering drugs including statins or the researchers did not declare whether lipid-lowering drugs were taken. The relationship between PCSK9 and BP could be influenced because lipid-lowering drugs including statins were demonstrated to play a role in BP and PCSK9 levels.[22,23] Furthermore, little information is currently available for the relationship between PCSK9 and BP in patients with hypertension to date. In addition, hypertension is considered as the major determinant of carotid artery intima–media thickness (cIMT) as an index of carotid atherosclerosis as well as artery stiffness,[24–28] whereas the level of cIMT is higher in normotensive offspring of hypertensive parents compared with those of normotensive parents.[29] Previous study showed a positive association of PCSK9 levels with cIMT in hypertensive patients, but in the study statins were taken.[30]

Hence, in the present study we aimed to detect the association between PCSK9 level and BP and IMT in patients without or with hypertension without lipid-lowering drug therapy.

METHODS
Study population
In the present study, consecutive patients hospitalized in our center were screened between October 2012 and October 2014 for the following inclusion criteria: not treated with lipid-lowering agents (statins, fibrates, nicotinic acid, ezitimibe and omega 3) for at least 3 months before the study and over the age of 18 years. Exclusion criteria were the existence of any infectious or systematic inflammatory diseases, significant hematologic disorders, thyroid dysfunction, severe liver and/or renal insufficiency and malignant tumors. According to the inclusion and exclusion criteria, a total of 805 patients were enrolled eligibly. Of these participants, 481 hypertensives and 324 normotensives were included, and the data of 256 patients for IMT were available. There were no significant differences in clinical characteristics between 256 participants who were enrolled in cIMT study and 549 participants who were not. The definition of hypertension was repeated SBP and/or DBP $\geqslant 140$ and/or $\geqslant 90$ mm Hg on at least two different occasions or currently using anti-hypertension drugs.[31,32] Coronary artery disease was diagnosed as the presence of coronary lesions $\geqslant 50\%$ at least one major epicardial artery segment assessed by at least two independent senior interventional cardiologists. Diabetes mellitus was defined as fasting glucose levels $\geqslant 7.0$ mmol l^{-1} in multiple determinations and/or was receiving at least one glucose-lowering treatment. The study was approved by the hospital ethical review board (Fuwai Hospital & National Center for Cardiovascular Diseases, Beijing, China), and all patients gave their written informed consent.

Biochemical determinations
Fasting blood samples were collected from all enrolled patients after hospitalization. The blood samples for the measurement of PCSK9 levels were stored at $-80\,^{\circ}\mathrm{C}$ until analysis. The concentrations of plasma triglyceride, total cholesterol, high-density lipoprotein cholesterol, LDL-C, apolipoprotein B, apolipoprotein A-I and fasting glucose were measured by automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). Hemoglobin A1c was examined using Tosoh Automated Glycohemoglobin Analyzer (HLC-723G8, Tokyo, Japan). PCSK9 levels in plasma were assayed using a high-sensitivity, quantitative sandwich enzyme immunoassay (Quantikine ELISA, R&D Systems Europe Ltd, Sweden) as described in our previous studies.[33,34] The minimum detectable dose of PCSK9 was 0.096 ng ml^{-1}.

Carotid ultrasonography assessment
Carotid ultrasound was evaluated as described previously.[35,36] Briefly, ultrasonic examinations of left and right carotid arteries were performed by two trained ultrasonographers who were blinded to participants' clinical characteristics using 128 System (Acuson, Mountain View, CA, USA) with a high-resolution 7.5–10.0 MHz transducer. IMT was measured at the far wall of three 10-mm segments of bilateral carotid artery: the proximal common carotid artery, the distal common carotid artery and the bifurcation. The largest IMT value was determined as the maximum IMT (max-IMT) and the average value of measured IMT as the mean IMT (mean-IMT). The average of right and left values was recorded as the individual representative value. The mean difference of IMT between two ultrasonographers was 0.036 mm.

Statistical analysis
Continuous variables are expressed as mean $\pm$ s.d. or median (interquartile range) and categorical variables as frequencies (percentage). Mann–Whitney test was applied for comparison of clinical parameters between the groups of patients with or without hypertension. The categorical variables were compared using the χ^2 test. The associations of PCSK9 with SBP, DBP, pulse pressure (PP), mean-IMT, max-IMT and other parameters were analyzed using Spearman's rank correlation and multiple linear regression. Two-sided *P*-values were considered statistically significant. Statistical analysis was performed with SPSS version 19.0 software (SPSS, Chicago, IL, USA).

RESULTS
Clinical and biochemical characteristics of patients with or without hypertension
The baseline characteristics of the cohort of 805 participants are shown in Table 1. There were higher values for age and body mass index as well as higher percentages of coronary artery disease and diabetes in hypertensives than in normotensives ($P < 0.01$). The levels of SBP, DBP and PP were higher in hypertensives than in normotensives, and higher levels of SBP and PP but lower levels of DBP in hypertensives were found in females than in males ($P < 0.01$ or 0.05). Compared with men, women in hypertensives or normotensives had higher levels of total cholesterol, high-density lipoprotein, LDL-C and apolipoprotein A-I ($P < 0.01$ or 0.05). In additionally, higher levels of total cholesterol, TG and LDL-C in women were found in normotensives than in hypertensives ($P < 0.01$ or 0.05), and it was likely because of current smoking status, the percentages of diabetes and coronary artery disease, hormone level, the usage of β-receptor blockers or dietary habits.[37–40] PCSK9 level was found higher in women than in men in patients with or without hypertension, consistent with previous studies,[18,19] but no significant difference in PCSK9 level was found between hypertensives and normotensives. Of the 256 patients for the study of the association between PCSK9 and IMT, the baseline clinical and biochemical characteristics are summarized in Supplementary Table 1.

Associations of plasma PCSK9 level with metabolism factors and BP
As shown in Table 2, a significant but weak positive correlation of PCSK9 level with age was found in hypertensives ($r = 0.099$, $P = 0.029$) but not in normotensives. PCSK9 level was not associated with TG and body mass index in both hypertensives and normotensives, consistent with previous studies[41–43] but contrary to some studies.[18,44] On the other hand, PCSK9 level was positively associated with LDL-C, apolipoprotein B, apolipoprotein A-I and hemoglobin A1c in both groups but high-density lipoprotein cholesterol in normotensives. No correlation between PCSK9 and SBP and DBP was found in all enrolled population, hypertensives or normotensives, whereas the level of PCSK9 exhibited a negative association with PP in normotensives. Meanwhile, we assessed the association between PCSK9 and BP according to sex in hypertensives and normotensives. However, there was still a lack of a correlation between plasma PCSK9 level and SBP and DBP in both hypertensives and normotensives regardless of sex (Figures 1 and 2). In addition, there was a significant

Table 1 Baseline characteristics and blood pressure levels between the hypertensives and normotensives according to sex

| Characteristics | Hypertensives (n = 481) | | Normotensives (n = 324) | |
	Male (n = 314)	Female (n = 167)	Male (n = 206)	Female (n = 118)
Age (years)	56.02±9.58	61.30±9.89[††]	53.44±11.08[**]	55.08±9.99[**]
Body mass index (kg m^{-2})	26.65±3.33	25.59±3.56[††]	24.97±3.44[**]	24.21±3.08[†,**]
Smoking, n (%)				
Current smokers	190 (60.5)	12 (7.2)	116 (56.3)	11 (9.3)
Former smokers	13 (4.1)	0	12 (5.8)	1 (0.8)
Never smokers	111 (35.4)	155 (92.8)	78 (37.9)	106 (89.8)
Diabetes, n (%)	88 (28.0)	44 (26.3)	30 (14.6)[**]	10 (8.5)[**]
CAD, n (%)	244 (78.0)	102 (63.0)[††]	137 (66.8)[**]	43 (36.4)[††,**]
Systolic blood pressure (mm Hg)	132.67±16.02	136.45±17.04[†]	119.82±11.47[**]	120.48±14.72[**]
Diastolic blood pressure (mm Hg)	82.37±12.05	79.36±12.48[††]	76.28±8.09[**]	75.25±8.57[**]
Pulse pressure (mm Hg)	50.30±12.91	57.09±14.66[††]	43.54±9.66[**]	45.23±11.69[**]
Antihypertensive agents, n (%)				
ACEI/ARB	85 (27.0)	35 (21.0)	0	0
β-Blockers	81 (25.8)	46 (27.5)	26 (12.6)	9 (7.6)
CCB	101 (32.2)	60 (35.9)	0	0
Left ventricular ejection fraction (%)	65.46±6.12	66.13±6.50	64.80±8.01	65.97±6.33
Left ventricular diastolic diameter (mm)	49.03±4.48	46.02±4.34[††]	47.82±5.12[**]	44.92±4.24[††,*]
Triglyceride (mmol l^{-1})	1.67 (1.23, 2.38)	1.69 (1.26, 2.44)	1.63 (1.12, 2.31)	1.59 (1.07, 2.20)[*]
Total cholesterol (mmol l^{-1})	4.79±1.03	5.04±0.94[††]	4.83±1.11	5.30±1.28[††,*]
LDL cholesterol (mmol l^{-1})	3.18±0.93	3.40±0.91[†]	3.28±1.04	3.66±1.26[††,*]
HDL cholesterol (mmol l^{-1})	1.03±0.29	1.16±0.34[††]	1.03±0.29	1.23±0.41[††]
ApoAI (mg dl^{-1})	1.31±0.26	1.44±0.31[††]	1.30±0.26	1.46±0.28[††]
ApoB (mg dl^{-1})	1.00±0.27	1.07±0.26[††]	1.03±0.31	1.07±0.33
Fasting glucose (mmol l^{-1})	5.72±2.11	5.65±1.53	5.51±1.78	5.22±1.05[**]
HbA1c (%)	6.28±1.02	6.29±0.96	6.10±1.17	5.91±0.82[**]
PCSK9 (ng ml^{-1})	212.89 (173.18, 262.85)	259.23 (207.25, 305.60)[††]	224.04 (185.60, 271.26)	246.89 (198.24, 304.09)[††]

Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ApoAI, apolipoprotein A-I; ApoB, apolipoprotein B; CAD, coronary artery disease; β-blockers, β-receptor blocker; CCB, calcium channel blocker; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PCSK9, proprotein convertase subtilisin kexin type 9.
Data presented as mean±s.d., n (%) or median (25th, 75th percentiles).
[†]$P<0.05$ and [††]$P<0.01$ in comparison with males of the same subgroup;
[*]$P<0.05$ and [**]$P<0.01$ in comparison with normotensive subgroup of the same sex.

Table 2 Correlation between PCSK9 and metabolic factors including SBP, DBP and PP

| | Overall (n = 805) | | Hypertension (n = 481) | | No hypertension (n = 324) | |
	r	P	r	P	r	P
Age	**0.068**	**0.052**	**0.099**	**0.029**	0.040	0.472
BMI	−0.042	0.234	−0.051	0.269	−0.002	0.966
TG	0.054	0.125	0.080	0.081	0.027	0.629
LDL-C	**0.251**	**<0.001**	**0.175**	**<0.001**	**0.364**	**<0.001**
HDL- C	**0.089**	**0.012**	0.052	0.257	**0.139**	**0.012**
ApoB	**0.227**	**<0.001**	**0.210**	**<0.001**	**0.252**	**<0.001**
ApoAI	**0.130**	**<0.001**	**0.125**	**0.006**	**0.138**	**0.013**
Glucose	0.067	0.059	0.028	0.540	0.104	0.060
HbA1c	**0.099**	**0.005**	**0.104**	**0.022**	**0.127**	**0.023**
SBP	−0.048	0.174	−0.010	0.819	−0.073	0.189
DBP	−0.033	0.346	−0.058	0.207	0.033	0.558
PP	−0.017	0.625	0.048	0.297	**−0.111**	**0.046**

Abbreviations: ApoAI, apolipoprotein A-I; ApoB, apolipoprotein B; BMI, body mass index; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin kexin type 9; PP, pulse pressure; SBP, systolic blood pressure; TG, triglyceride.
Data in bold represent significant correlations.

correlation of PCSK9 with PP only in female normotensives (Figure 2).

Correlation of PCSK9 levels with cIMT
In the cohort of 256 participants, PCSK9 levels were positively associated with mean-cIMT ($r=0.206$, $P=0.020$) and max-cIMT ($r=0.186$, $P=0.036$) in hypertensives but not in all enrolled population and normotensives (Figure 3). However, this positive association was not found after adjusting for age, sex and body mass index (Table 3). Similarly, PCSK9 level was found to be positively associated with mean-cIMT ($r=0.297$, $P=0.011$) and max-cIMT ($r=0.288$, $P=0.013$) in male hypertensives but not in female hypertensives, whereas such positive associations were absent after adjusting for age ($P>0.05$). In addition, we examined the link of PCSK9 with cIMT under different status of BP control in hypertensives. Under the status of controlled BP (SBP <140 mm Hg and DBP <90 mm Hg), PCSK9 levels showed a positive correlation with max-cIMT, whereas there was a tendency for a positive association between PCSK9 and mean-cIMT (Supplementary Table 2). Nevertheless, such a positive association disappeared after adjusting for age ($\beta=0.034$, $P=0.152$). Under the status of uncontrolled BP (SBP ≥140 mm Hg or
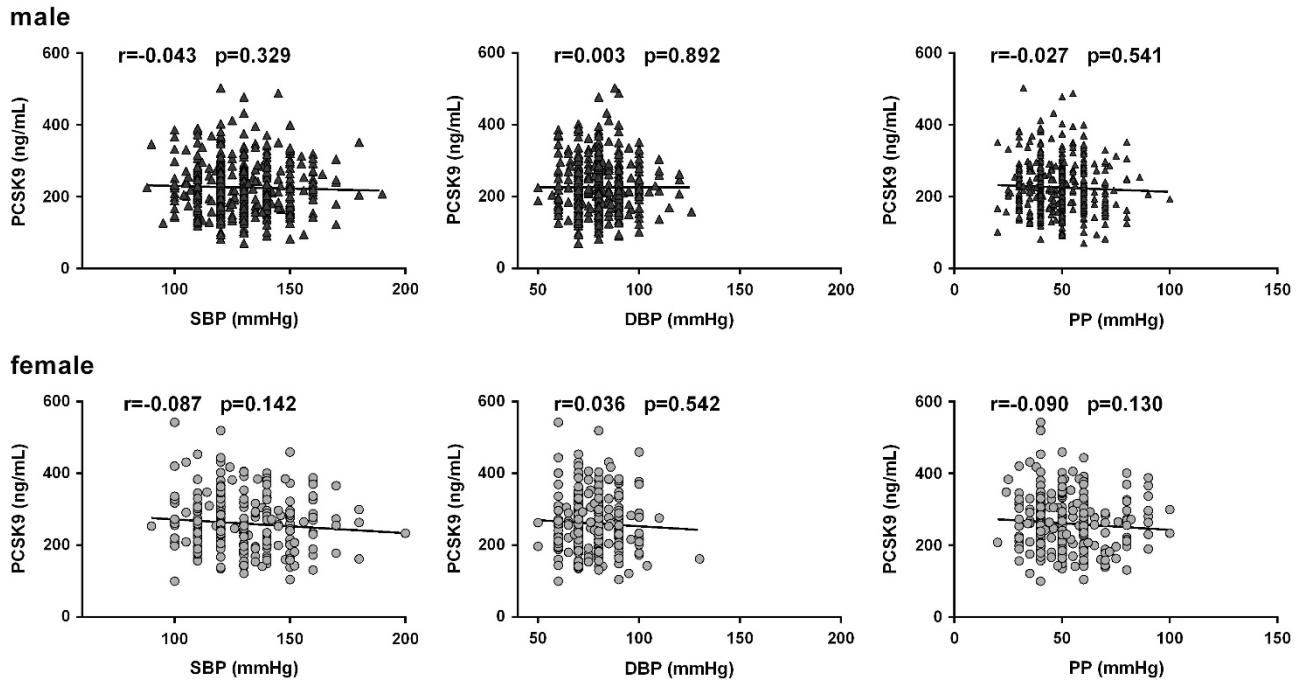
male

female

Figure 1 Association of proprotein convertase subtilisin kexin type 9 (PCSK9) level with systolic blood pressure (SBP), diabolic blood pressure (DBP) and pulse pressure (PP) in male or female hypertensives.
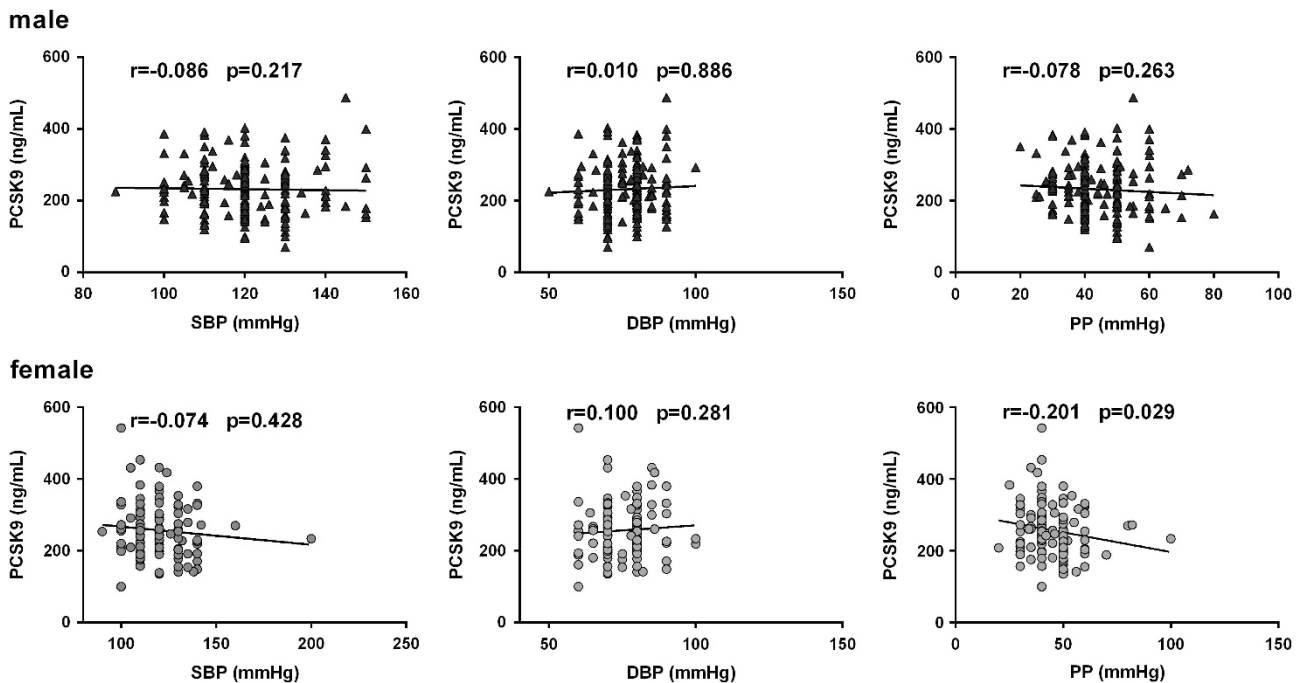
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Figure 2 Relation of proprotein convertase subtilisin kexin type 9 (PCSK9) level to systolic blood pressure (SBP), diabolic blood pressure (DBP) and pulse pressure (PP) in normotensives according to sex.

DBP $\geqslant$ 90 mm Hg), there was no relation of PCSK9 to mean- or max-cIMT (Supplementary Table 2).

DISCUSSION

In the present study, we found that plasma PCSK9 levels were not associated with SBP, DBP and PP in patients with or without hypertension. Besides, we also found that PCSK9 level was not

associated independently with cIMT in hypertensives. To our knowledge, this is the first study to investigate the relationship between PCSK9 level and BP and cIMT in hypertensive and normotensive patients who were not under lipid-lowering drugs.

Our results are inconsistent with previous epidemiological studies concerning the relationship between PCSK9 levels and BP. For instance, in Dallas Heart Study, Lakoski et al.[18] reported that PCSK9
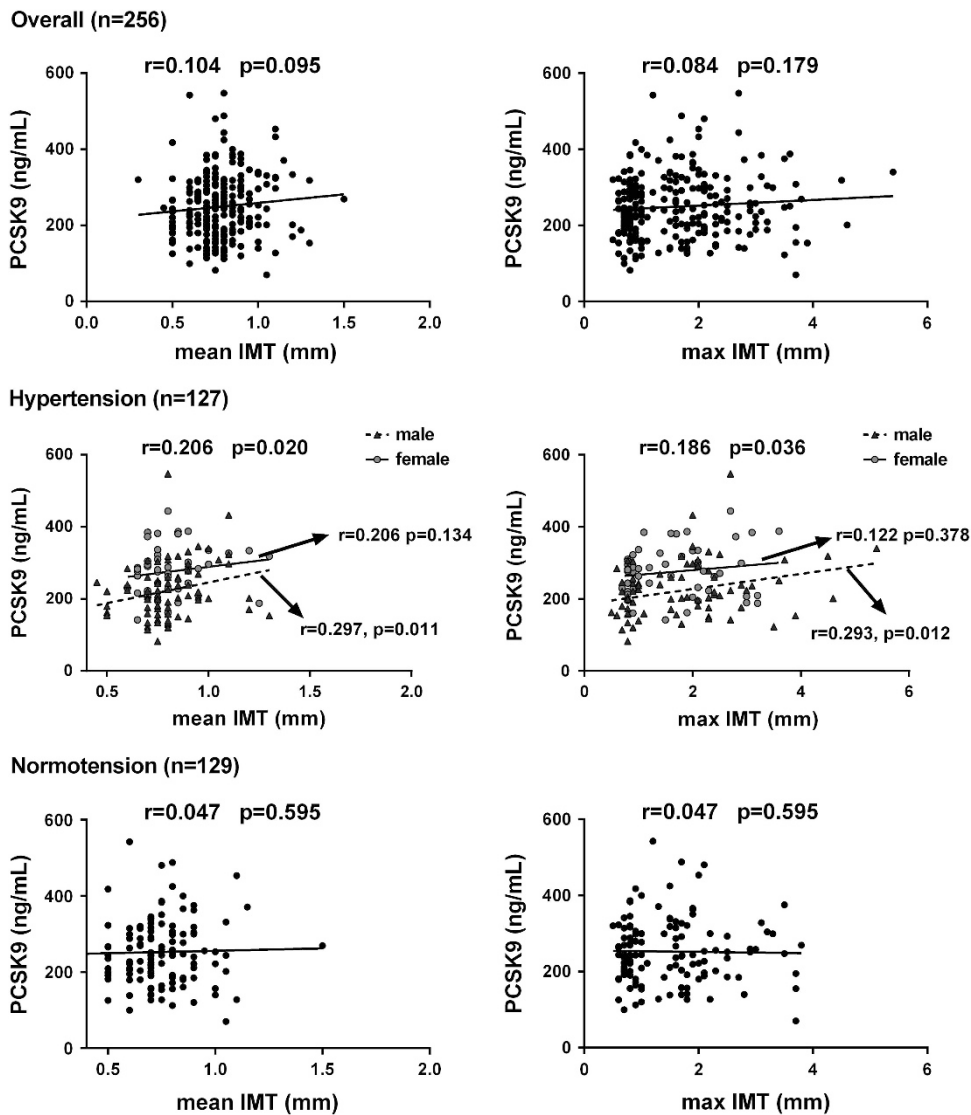
Figure 3 Association of plasma proprotein convertase subtilisin kexin type 9 (PCSK9) level with carotid mean intima–media thickness (mean-IMT) and maximum (max)-IMT in overall subjects, hypertensives and normotensives.

Table 3 Multiple regression models dependent on PCSK9[a]

Variables	Standardized coefficients	95% CI	P-value
Age	0.213	(0.019, 0.408)	0.032
Sex	0.303	(0.124, 0.482)	0.001
BMI	0.060	(−0.101, 0.222)	0.460
LDL-C	0.167	(0.005, 0.329)	0.044
SBP	−0.127	(−0.339, 0.085)	0.237
DBP	−0.016	(−0.234, 0.202)	0.885
Mean-IMT	0.044	(−0.138, 0.225)	0.636
Max-IMT	0.126	(−0.064, 0.315)	0.193

Abbreviations: BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; IMT, intima–media thickness; LDL-C, low-density lipoprotein cholesterol; Max-IMT, maximum-IMT; PCSK9, proprotein convertase subtilisin kexin type 9; SBP, systolic blood pressure. Multiple linear regression analysis was performed. The regression equation included age, sex, body mass index, history of hypertension, systolic blood pressure, diastolic blood pressure LDL-C, mean-IMT and max-IMT.
[a]Log-transformed data.

levels were positively associated with SBP and DBP in women but not in men in both African Americans and European Americans. In parallel, Cui *et al.*[19] showed a positive association of PCSK9 with SBP and DBP in both men and women in Han Chinese population by univariate analysis, but in a multiple regression analysis the positive correlations of PCSK9 with SBP in women and DBP in men were not found. In those studies, healthy participants were enrolled, whereas in the present study we investigated the relationship between PCSK9 levels and BP in hypertensives. In our study we found no association of PCSK9 with SBP, DBP and PP in patients with or without hypertension. Furthermore, the similar results were found in sex subgroup except the negative association between PCSK9 and PP in normotensive women. Moreover, Cariou *et al.*[45] reported that a positive correlation of PCSK9 concentrations with SBP but not DBP was found in diabetic patients by univariate analysis, but the correlation was absent in a multiple regression analysis.

On the other hand, our finding is in agreement with some studies. A recent study with a large cohort of >28 000 initially healthy

American women did not exhibit an association between PCSK9 levels and SBP and DBP.[21] Previous *in vitro* study showed that PCSK9 downregulated epithelial Na^+ absorption by reducing the epithelial Na^+ channel expression, and the researchers speculated that PCSK9 could contribute to BP control and a decrease in PCSK9 level would raise the risk of hypertension.[46] However, Berger et al.[20] found that PCSK9 deficiency did not alter BP and sodium homeostasis in mouse models of hypertension, supporting our finding. Furthermore, several clinical trials concerning anti-PCSK9 monoclonal antibodies have not shown available date on BP and no adverse events linked to hypertension have been reported.[47–49] Our previous studies also indicated no association of PCSK9 level with BP in patients with coronary artery disease.[50–52] In addition, clinical rare patients with undetectable PCSK9 level did not exhibit an influence on BP.[53–55]

Previous gene studies of PCSK9 revealed that hypertension was less common in the carriers of PCSK9 (Y142X, C679X) compared with noncarriers.[56] Moreover, the interaction of PCSK9 AG genotype and cigarette smoking decreased SBP, whereas the interaction of PCSK9 AA genotypes and cigarette smoking increased DBP levels in Chinese Minority of Zhuang.[57] In our study, we found no difference in the association of PCSK9 with SBP and DBP under different smoking status (data not shown), in accordance with previous study.[21] We speculated that the difference could have resulted from different gene styles of PCSK9 from different study populations.[58]

Hypertension is demonstrated as the key determinant of cIMT.[24] Hence, in our study we also investigated the association between PCSK9 level and cIMT. We found that PCSK9 levels were positively associated with both mean-cIMT and max-cIMT in hypertensives but not in normotensives, in accordance with previous study by Lee et al. Nevertheless, to be inconsistent with the results of Lee et al.,[30] we found that these positive associations were absent after adjusting some risk factors of cardiovascular disease such as age and sex, which is supported by the recent study from Zhu et al.[59] Zhu et al. reported that PCSK9 level was related to cIMT ($\beta = 0.073$, $P = 0.005$) but it was not an independent predictor of cIMT in backward multiple regression models in the cohort consisting of 1527 middle-aged men who were free of vascular diseases. Nevertheless, in the cohort from Zhu et al.,[59] 26% of the participants were patients with hypertension and 8% were on statin therapy. In the present study, we found that PCSK9 level was positively associated with cIMT in hypertensives but such a positive association was absent after adjusting for age. To be different from the study by Lee et al.,[30] the participants in our study were not treated by lipid-lowering drugs that can increase PCSK9 level[22]. Moreover, the hypertensives were younger in our study compared with those in the study by Lee et al.,[30] whereas cIMT is associated with age.[60] All these could account for the difference in results. Furthermore, the significantly positive association between PCSK9 and cIMT was found in male hypertensives, whereas in female hypertensives there was a positive tendency for the association of PCSK9 with IMT that may result from the smaller sample of females. Interestingly, the positive association between PCSK9 and cIMT in male hypertensives was absent after adjusting for age. Similarly, the positive association between PCSK9 and cIMT in hypertensive patients with controlled BP disappeared after adjusting for age. In addition, previous study showed that mean-IMT was reduced in PCSK9 loss-of-function variant carriers when compared with noncarriers,[56] supporting our finding. In view of the positive association of PCSK9 with cIMT, we speculate that PCSK9 inhibitor could reduce carotid artery atherosclerosis. Thus, our finding is partly inconsistent with the study by Lee et al.[30] but is supported by Zhu et al.[59] However, further study is required to clarify this issue, and whether PCSK9 inhibitors reduce cIMT also needs further research.

Despite negative results concerning the relationship between PCSK9 levels and BP, our finding deserves interest. As serum LDL-C levels are demonstrated to be associated with hypertension and BP values, the promising lipid-lowering drug PCSK9 inhibitor could play some role in BP or onset of hypertension. Thus, it is vital to address the issue. Although some studies have been performed, the relationship between PCSK9 and BP is not well established. Our finding supports the viewpoint that PCSK9 could not affect BP. Of course, the possibility could not be excluded that the PCSK9 activity may be more relevant than its level in determining the BP values as well as LDL-C level, and it requires further study. However, the ongoing large-scale studies about PCSK9 inhibitors will help to clarify this issue.

Our study has several limitations. First, the association between PCSK9 level and one-time levels of SBP or DBP was investigated, but BP values are easy to fluctuate and we did not show the relationship between mean BP values over a period of time and PCSK9 level because of the lack of concerning data. Second, although our data did not show an association between PCSK9 levels and BP values, we did not exclude a possibility that PCSK9 activity may be more relevant than its level in determining the BP values. Finally, our study sample is relatively small.

CONCLUSION

Our data showed that PCSK9 levels are not associated with BP in hypertensives or normotensives, suggesting that the ongoing development of PCSK9 inhibitors could have no effect on BP. In addition, our results exhibited a positive association between PCSK9 and cIMT in univariate but not multivariate analyses. Thus, whether a decrease in PCSK9 level or PCSK9 inhibitors could reduce carotid atherosclerosis in patients with hypertension requires further researches.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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